Brain Tumors (Medhkour): WS and Study Guide

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Use this guide and worksheet to go through the lecture. Answers can be found in the lecture handout. In general, I recommend focusing on the things Medhkour emphasized in lecture. For example, understand how tumor suppressor genes work (or fail to work), as well as the major ones he mentioned. Know what's more common in children vs. adults. Compare supratentorial and infratentorial tumors. Finally, know the targets of management and therapeutics.

Brain tumor (BT)	
Clinical definition	**Cellular definition**

Definitions:

Immunological and Chromosomal Changes:

- Set of epitopes that distinguishes neoplastic from normal cells (antibody-immune response)
- _____ w/ aneuploid or polyploidy abnormalities
- Chromosomal segments that may be _____, _____, or _____

Genetics:

- Alterations in DNA sequence changes the expression of genes that regulate _____
- Alterations of _____ that encode protein structures

Molecular Genetics & Tumors:

- Genetic changes underlie _____ progression of tumor malignancy
- Genetic _____ should correlate with tumor clinical behavior
- ***Future of therapeutic interventions lies in development of mechanisms that reverse or interrupt the cycle of genetic changes***

Oncogenes:

- Promote tumor growth via _____ signals
- One single mutation required to activate oncogene – rare event
- E.g.: Glioblastomas (GBM):
    - Epidermal growth factor receptors (EGFR) are amplified and play important role in tumor behavio

Tumor Suppressor Genes:

- Restrain growth or promote terminal differentiation of cells
- Sustain an inactivating mutation or deletion of one copy of the gene which leads to removal of the brakes on cell growth and division
- E.g.: *PTEN* tumor suppressor gene
    - Located on chromosome 10
    - Normal tumor suppressing functions:
        - *PTEN* product encodes lipid phosphatase and down-regulation of phosphatidylinositol levels
        - Activates _____, pathway responsible for *PTEN*'s tumor suppressive function
    - Inactivation:
        - 25-40% of GBMs
        - High rate of mutation in high grade GBM
        - Correlated with poor outcome
    - Therapeutics
        - Molecular targets directed against *PTEN/Akt* pathway

Classification of Brain Tumors

Classification of Brain Tumors		
Microscopic histology	**Brain tumors** – tumors in the brain ***Metastasis*: most common (over half); originated elsewhere** List some e.g.:	**Gliomas** – tumor starts in brain or spine ***GBM*: most common of the gliomas (half)** Others besides GBM:

Prevalence, Incidence, and Mortality Rates of Brain Tumors

Prevalence	
Incidence	
Mortality	

Determinants of Incidence of Specific Tumor Types

- **Adults**:
  - _____ tumors are the most common brain tumor
  - _____ and _____ are the most common
- **Children**:
  - Brain tumors are most common _____ tumor
  - _____ and _____ are the most common types

Brain Tumor Metastasis

- Most common metastasis (M and F): _____
  - 2nd most common in F: _____
- Other most common (M and F): melanoma, renal or colon

Therapeutic targeting of oncogenes:

- Identify molecular changes that drive tumor growth
- Target these altered genes pharmacologically
- Still difficult to suppress because of new mutation and evasion of therapy
- Currently, therapy is targeting genes involved in multiple cancers, e.g. _____, _____, _____, _____

General Management of BTs

- _____
  - Very effective in metastatic tumors
  - Modest response in primary gliomas
  - Prophylactic usage of anto-convulsants is not routine
- _____
  - Can be aggressive resection for chemo delivery
- **Radiotherapy**
- _____
  - Get past BBB
  - Agents disrupt BBB (Manitol)
- **Radiosurgery**
- **Repeat surgery**

Other Technological Advances

- _____ (SSEP's) to asses what area to avoid
- Stealth system for stereostatic free-hand guidance system
- Endoscopy
- Intra-operative MRI is expensive, could just improve on ultrasound
- _____ prior to surgery to asses function
- _____ for diagnosis of tumor type, abscess, necrosis, etc.

General Clinical Aspects of Brain Tumors:

Clinical Aspects	
Supratentorial Tumors	**Infratentorial Tumors**
Cerebral hemispheres, diencephalon • ICP • Hydrocephalus • Progressive neurological deficit • Headaches • TIA-like symptoms (hemorrhage or occlusion by tumor) • Endocrine disturbance • CSF leak (pituitary adenomas)	**Brainstem and cerebellum** • ICP and headache • N/V • Papiledema • Gait disturbance (ataxia) • Vertigo • Diploplia

Supratentorial Tumors	Infratentorial Tumors
Herniation Brain pain due to innervation of dura by CN V; dural distension creates headaches	No room for movement, much smaller Nausea and vomiting to be taken seriously
E.g. GBM, meningiomas, familial brain tumors (phakomatosis), pituitary tumors (adenomas)	AKA Posterior fossa; e.g. medulloblastoma, (juvenile) pilocytic astrocytoma

Supratentorial Tumors	
Glioblastoma Multiforme (GBM)	• Most aggressive brain tumor (most common glioma) o Presents in the _____ (age where it presents) o Survival 6-18 months o Affects eloquent area • Classical histological features: o _____ o _____ _____ (neovascularization) o _____ (especially in center) o _____ (abnormal size and shape, pigmentation) • Tumor suppressor genes: _____, _____, _____ • Treatment: o Surgery (aggressive resection), chemotherapy, radiation, repeat surgery
Meningiomas	• 2nd most common _____ primary brain tumor (after astrocytomas) • Arises from _____ cells • Rarely invades cortex • Can be malignant by locations • Tumor suppressor: _____
_____ **tumors**	Phakomatosis • Neurofibromatosis 1 (chromosome 17) and 2 (chromosome 22) *NF 1 and NF2* • Tuberous sclerosis • Von Hippel-Landau
_____ **tumors**	Pituitary adenoma • More common in F, particularly African American

Infratentorial Tumors	
Posterior Fossa Tumors	• Children: common o Medulloblastomas, astrocytomas, ependymomas • Adults o Male: _____ o No seizures
_____	• Malignant • Associated with _____: CSF not draining • Treatment: o Do we shunt hydrocephalus? *No, we do surgery* o Surgery, chemotherapy, radiation therapy
_____ **astrocytoma**	Juvenile • Is it curable? *Yes* • Treatment: *Remove associated nodule*